REMARKS

Status of the Claims

Claims 1-21, including independent claim 1, are pending in this application, with claims 22-43 being in a withdrawn state. In light of the amendments and remarks contained herein, reconsideration of claims 1-21 is respectfully requested.

Patentability of Claims 1-21

A. Nonobviousness in light of Vyakarnam, Albrecht, and Naughton

Claims 1-21 currently stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,534,084 to Vyakarnam et al. (herein "Vyakarnam"), in view of a journal article of Albrecht et al., "Closure of Osteochondral Lesions Using Chondral Fragments and Fibrin Adhesive," *Arch Orthop Trauma Surg*, 101:213-217 (1983) (herein Albrecht), and U.S. Patent No. 5,842,477 to Naughton et al. (herein "Naughton"). The claims, however, are all patentable because none of the cited art teaches the element of "a plurality of biocompatible, bioresorbable granules" as recited in the claims.

Independent claim 1 is drawn to a tissue repair implant that comprises a tissue carrier matrix. The tissue carrier matrix includes a plurality of biocompatible, bioresorbable granules, and at least one tissue fragment. The tissue fragment(s) have an effective amount of viable cells that can migrate out of the tissue fragment and populate the tissue carrier matrix. Such a matrix may have advantageous features. For example, the matrix can be in the form of an injectable suspension that can be delivered to a target site in a minimally invasive procedure (see U.S. Patent Application Publication No. US 2005/0113937 A1, corresponding to the published version of the present application (herein the "Published Application"), paragraph [0028]). Such an injectable suspension can be delivered to a tissue injury site; the suspension can then set or cure into a shape complementary to the defect site *in situ* (see id., paragraph [0060]). In such an instance, the granules may serve to provide sufficient mechanical integrity for cellular integration during tissue remodeling (see id., paragraph [0028]).

In contradistinction, none of the cited art teaches or suggests a tissue carrier matrix that includes a plurality of biocompatible, bioresorbable granules. Vyakarnam is directed to

biocompatible scaffolds having a gradient in composition or microstructure. As disclosed, the foam-like structures that act as Vyakarnam's scaffolds are first formed from various polymer solutions using techniques such as lyophilization, supercritical solvent foaming, gas injection extrusion, gas injection molding or casting (see Vyakarnam, column 12, lines 20-25; column 22, lines 10-47 (describing the use of a freeze-drier)). Subsequently, to seed cells in the scaffold, the formed foam structure "would be placed in cell culture and the sells seeded onto or into the structure" (see id., column 19, lines 10-11). That is, Vyakarnam is no way contemplates or hints of formulating or utilizing "a tissue carrier matrix comprising a plurality of biocompatible, bioresorbable *granules* and at least one tissue fragment" consistent with claim 1. Though the Office Action suggests that the polymeric material can be suitable for an injectable tissue carrier matrix, the reference neither teaches *granules* nor tissue fragments in a tissue carrier matrix.

Albrecht also lacks any teaching of the presence of biocompatible, bioresorbable granules in a tissue carrier matrix as recited in claim 1. The reference discloses a study that includes experimental results of injecting a mixture of "very small autologous cartilage fragments and a special fibrin adhesive" into knee joints of adult rabbits (see Albrecht, page 215, left hand column). Clearly, there is no disclosure of biocompatible, bioresorbable granules that are combined with at least one tissue fragment to form the tissue carrier matrix of claim 1.

Though the Office Action suggests that Albrecht teaches "collagen foam particles mixed with fibrin glue . . ." (see Office Action, page 7, last full paragraph), this is clearly not the case. Indeed, what is disclosed is the use of a "heterologous collagen *foam*" (see Albrecht, page 214, right hand column – under Group II and III); this is distinct from the *granules* recited in claim 1. Furthermore, Albrecht in no way teaches the use of the collagen foam with cartilage fragments. As disclosed in the *Methods and Materials* section, the only uses of collagen foam are in Group II, where the foam is added to a hole alone, and in Groups III and V, where the foam is used to stop bleeding before the hole is filled with either fibrin or a bolus of Group IV (see id.). There is no hint or suggestion of combining the foam with cartilage fragments. Accordingly, in no way does Albrecht suggest or hint of the tissue carrier matrix recited in claim 1.

Finally, Naughton also fails to teach or suggest the biocompatible, bioresorbable granules recited in claim 1. Naughton teaches methods of repairing cartilage by forming a

three-dimensional scaffold outside the body from a variety of man-made or natural materials, preferably in the form of a felt composed of a multifilament yarn, sponge, a braid or woven threads (see Naughton, from column 6, line 50 to column 7, line 59). Following scaffold formation, the scaffold is implanted into the defect site (see id., column 9, lines 30-35). Stromal cells are seeded into the defect site either before or after scaffold insertion (see id., column 17, lines 6-11). Accordingly, like Vyakarnam, Naughton fails to suggest or even hint of a tissue carrier matrix including either biocompatible, bioresorbable granules or at least one tissue fragment as recited in claim 1.

Therefore, none of the cited art teaches or suggests a tissue carrier matrix comprising a plurality of biocompatible, bioresorbable granules and at least one tissue fragment consistent with claim 1. "To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art" (see MPEP §2143.03 citing *In re Royka*, 490 F.2d 981 (CCPA 1974)). Accordingly, the cited art cannot sustain a *prima facie* case of obviousness. Claim 1 is patentable.

Claims 2-21 ultimately depend from claim 1. Accordingly, each of these claims is patentable for at least the same reasons that claim 1 is patentable. Furthermore, the dependent claims are also patentable for other independent reasons. For example, beyond not teaching or suggesting the tissue carrier matrix of claim 1, none of the cited art suggests the tissue carrier matrix in the form of an injectable suspension as recited in claim 2. As well, none of the art cited teaches or suggests the tissue particles sizes of claim 5. Since none of the art teaches the granules of claim 1, the art also does not disclose the average maximum outer diameter of the granules (claim 8), granules that are porous (claim 9), granules with surface roughness (claim 10), and biological components contained within the granules (claim 20) or contained within a coating of the granules (claim 21). The cited art also does not teach or suggest the use of a biological component comprising platelets and an activator of platelets (claims 17-18).

The Office Action suggests that the recitations of claim 5, 8-10, and 21 are just a matter of routine optimization since Vyakarnam and Naughton disclose porous scaffold/matrix materials with similar particle sizes and diameters. This mischaracterizes the teachings of Vyakarnam and Naughton since neither reference in any way discusses the use of *granules* in

any way. The references only discuss the *pore size* or *mesh size* of a *scaffold*, not the size of *granules* in a tissue carrier matrix or any other properties of granules. Furthermore, though the Office Action suggests that Albrecht and Naughton disclose the use of biological components, such components are utilized only with respect to a scaffold and not granules in a tissue carrier matrix. Accordingly, the cited art also fails to teach or suggest many of the recitations of dependent claims 2-21.

In summary, claims 1-21 are patentable over any combination of Vyakarnam, Albrecht, and Naughton.

B. Double Patenting

Claims 1-21 currently stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,884,428 B2 to Binette et al. (herein the "'428 patent"). The pending claims, however, are not obvious because they are patentably distinct relative to the issued claims of the '428 patent. As previously discussed, claim 1 is directed to a tissue repair implant that comprises a tissue carrier matrix, which includes a plurality of biocompatible, bioresorbable *granules*, and at least one tissue fragment. Independent claim 1 of the '428 patent is directed to an implant having a bioabsorable polymeric foam component, a reinforcing component formed of a mesh-containing material, and at least one biological component; claims 2-19 of the '428 patent are all dependent from claim 1. Accordingly, claim 1 of the present application is patentably distinct from the claims of the '428 patent at least because of the *granules* recited in the claim. Claims 2-21 of the present application are accordingly also non-obvious at least for the same reason that pending claim 1 is distinct. Therefore, claims 1-21 should be patentable over the claims of the '428 patent.

Claims 1-21 also stand provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-35 of copending U.S. Patent Application Serial No. 10/374,772. As well, claims 1-21 are also provisionally rejected for nonstatutory double patenting as being unpatentable over claims 1-32 of copending U.S. Patent Application Serial No. 10/374,754. Pursuant to MPEP §804 I. B., and in light of the

arguments presented herein, Applicants request that the provisional obviousness-type rejections be withdrawn since the provisional double patent rejections are the only rejections remaining in the present application. As well, Applicants contend that the pending claims do not conflict with the claims of either cited pending application.

Accordingly, claims 1-21 are patentable over the double patenting rejections presented in the Office Action.

CONCLUSION

In view of the remarks above, Applicants submit claims 1-21 are in condition for allowance, and allowance thereof is respectfully requested. If the Examiner believes that an interview would facilitate the resolution of any outstanding issues, he is kindly requested to contact the undersigned.

Dated: October 25, 2006

Respectfully submitted,

Charlton Shen, Reg. No. 54,442
Attorney For Applicants
NUTTER MCCLENNEN & FISH, LLP
World Trade Center West
155 Seaport Boulevard
Boston, Massachusetts 02210-2604
Tel. (617) 439-2782
Fax (617) 310-9782

1552909.1